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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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<input type="checkbox"/>	<input type="checkbox"/>	EXAMINER
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ART UNIT	PAPER NUMBER
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28

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No. <b>08/914,332</b>	Applicant(s) <b>Van Arsdell et al.</b>
	Examiner <b>Peter Tung</b>	Art Unit <b>1652</b>
<i>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</i>		
<b>Period for Reply</b>		
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.		
<ul style="list-style-type: none"> <li>- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.</li> <li>- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.</li> <li>- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.</li> <li>- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).</li> <li>- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).</li> </ul>		
<b>Status</b>		
1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Aug 11, 2000</u>		
2a) <input type="checkbox"/> This action is <b>FINAL</b> .      2b) <input checked="" type="checkbox"/> This action is non-final.		
3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11; 453 O.G. 213.		
<b>Disposition of Claims</b>		
4) <input checked="" type="checkbox"/> Claim(s) <u>1-31</u> is/are pending in the application.		
4a) Of the above, claim(s) <u>23-31</u> is/are withdrawn from consideration.		
5) <input checked="" type="checkbox"/> Claim(s) <u>2 and 4-6</u> is/are allowed.		
6) <input checked="" type="checkbox"/> Claim(s) <u>1, 3, 7, 8, and 11-22</u> is/are rejected.		
7) <input checked="" type="checkbox"/> Claim(s) <u>9 and 10</u> is/are objected to.		
8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.		
<b>Application Papers</b>		
9) <input type="checkbox"/> The specification is objected to by the Examiner.		
10) <input type="checkbox"/> The drawing(s) filed on _____ is/are objected to by the Examiner.		
11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved.		
12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.		
<b>Priority under 35 U.S.C. § 119</b>		
13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).		
a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of:		
1. <input type="checkbox"/> Certified copies of the priority documents have been received.		
2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____.		
3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).		
*See the attached detailed Office action for a list of the certified copies not received.		
14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).		
<b>Attachment(s)</b>		
15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)		
16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)		
17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____		
18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____		
19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)		
20) <input type="checkbox"/> Other: _____		

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### **DETAILED ACTION**

1. Based upon the new grounds of rejection, the finality of the previous Office action is hereby withdrawn.
2. Claims 1-31 are pending.
3. Claims 23-31 are withdrawn from further consideration as being drawn to a non-elected invention.

#### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1, 3, 7 and 11-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Bower et al. (U.S. Patent No. 6,057,136). With regard to claims 1, 3, 7, 11 and 12, Bower et al. teach (col. 29, line 62 - col. 31, line 15) a method of producing the biotin vitamers biotin and dethiobiotin by culturing strain BI282, which contains BioW, BioA, BioB and BioD DNA, in a rich medium and isolating the biotin vitamers. The medium used in the production of biotin comprises veal infusion broth and yeast extract, which would be expected to provide at least 10 mmoles per liter of lysine or a lysine precursor. Although Bower et al. do not teach that strain

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BI282 comprises a lysine-utilizing DAPA aminotransferase, BI282 comprises DNA encoding a *B. subtilis* DAPA aminotrasferase which inherently uses lysine as an amino group donor.

With regard to claims 13-19, 21 and 22, Bower et al. teach (col. 21, lines 20-56; col. 22, Table 5) a method of producing the biotin vitamers biotin and dethiobiotin by culturing *E. coli* strain MM294 (wild type for bio genes) transformed with plasmid pBIO289, which contains BioW, BioA, BioB and BioD DNA, in a rich medium and isolating the biotin vitamers. A rich medium would be expected to contain methionine as well as provide at least 10 mmoles per liter of lysine or a lysine precursor. Although Bower et al. do not teach that the BioA of pBIO289 encodes a lysine-utilizing DAPA aminotransferase, the encoded *B. subtilis* DAPA aminotrasferase would inherently use lysine as an amino group donor. Additionally, the *E. coli* strain MM294 encodes a SAM-utilizing DAPA aminotransferase.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

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the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bower et al. (U.S. Patent No. 6,057,136) as applied to claims 1 and 3 above, and further in view of Yamada et al. (U.S. Patent No. 4,563,426, cited in previous Office action). The teaching of Bower et al. have been discussed supra. Bower et al. do not teach converting the recovered dethiobiotin to biotin by an additional fermentation. Yamada et al. teach (col. 1, lines 40-66) a method of producing biotin by adding dethiobiotin to a fermentation medium. Yamada et al. do not teach dethiobiotin production. It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce dethiobiotin, as taught by Bower et al., and to convert the dethiobiotin into biotin as taught by Yamada et al., for the benefit of producing biotin. One of ordinary skill in the art is motivated to combine the teachings as Bower et al. show a method of making dethiobiotin and the teachings of Yamada et al. show that dethiobiotin can be used to produce biotin. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the teachings of Bower et al. show a method of making dethiobiotin, which is a starting material for producing biotin, according to the method taught by Yamada et al. Therefore the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made.

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8. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bower et al. (U.S. Patent No. 6,057,136) as applied to claims 13 above, and further in view of Yamada et al. (U.S. Patent No. 4,563,426, cited in previous Office action). The teaching of Bower et al. have been discussed supra. Bower et al. do not teach converting the recovered dethiobiotin to biotin by an additional fermentation. Yamada et al. teach (col. 1, lines 40-66) a method of producing biotin by adding dethiobiotin to a fermentation medium. Yamada et al. do not teach dethiobiotin production. It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce dethiobiotin, as taught by Bower et al., and to convert the dethiobiotin into biotin as taught by Yamada et al., for the benefit of producing biotin. One of ordinary skill in the art is motivated to combine the teachings as Bower et al. show a method of making dethiobiotin and the teachings of Yamada et al. show that dethiobiotin can be used to produce biotin. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the teachings of Bower et al. show a method of making dethiobiotin, which is a starting material for producing biotin, according to the method taught by Yamada et al. Therefore the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made.

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***Allowable Subject Matter***

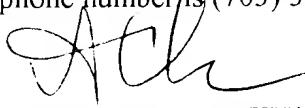
9. Claims 2, 4, 5 and 6 are allowed. The prior art of record does not teach or suggest a method of producing a biotin vitamer using a bacterium which is deregulated with respect to lysine production and which comprises a lysine-utilizing DAPA aminotransferase. While bacteria which overproduce lysine are known in the art, one of ordinary skill in the would not have been motivated to use these bacteria or these bacteria comprising a lysine-utilizing DAPA aminotransferase in the production of biotin vitamers.

10. Claims 9 and 10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
PONNATHAPU ACHUTAMURTHY  
SUPERVISOR, BIOLOGICAL PATENTS  
TELEPHONE: (703) 308-3804